Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (original) Crystalline LBD of RORα.

2. (original) The crystalline LBD of RORα of claim 1 wherein said LBD of RORα is associated with a small molecule.

3. (currently amended) The crystalline LBD of RORα of claim 1 ~~or 2~~ wherein said LBD of RORα is associated with a lipophilic substance.

4. (currently amended) The crystalline LBD of RORα of claim ~~1,~~ 2 ~~or 3~~ wherein said ~~LBD of RORα is associated with~~ lipophilic substance is cholesterol or a derivative of cholesterol.

5. (currently amended) The crystalline LBD of RORα of ~~any of the previous~~ claim~~s~~ 1 wherein said crystal comprises a unit cell having the dimensions of a=55.9 Å ± 2 Å, b=49.9 Å ± 2 Å, c=60.7 Å ± 2 Å and β=98.7°±5° and space group P2(1).

6. (currently amended) The crystalline LBD of RORα of ~~any of the previous~~ claim~~s~~ 1 wherein said crystalline LBD of RORα comprises the atomic structure coordinates of Table 8 or 9 or a part thereof.

7. (currently amended) A heavy atom derivative of a crystal according to ~~any of the previous~~ claim~~s~~ 1.

8. (original) A computer readable medium comprising a model embodying the structure of the LBD RORα comprising one or more sets of atomic coordinates in Table 8 or 9.

9. (currently amended) A method for identifying a substance binding to the LBD of RORα, comprising:
   (a) ~~providing~~ contacting a candidate substance with a model embodying the structure of the LBD of RORα comprising one or more sets of atomic coordinates in Table 8 or 9;
   (b) assessing the interaction of ~~a~~ said candidate substance with said model, and;
   (c) selecting a substance which is predicted to interact with the LED of RORα.

10. (canceled)

11. (currently amended) A method according to claim 9 ~~or 10~~ wherein the substance interacts directly or indirectly with one or more amino acids selected from the group consisting of:
Cys321, Gln322, Tyr323, Leu328,Trp353, Cys356, Ala357, Lys359, Ile360, Glu362,Ala363, Val397, Phe398, Arg400, Met401, Arg403, Ala404, Val412, Tyr413, Phe414, Phe424, Leu427, Cys429, Phe432, Ile433, Val436, His517, Lys520 and Tyr540.

12. (currently amended) A method according to claim 9 ~~or 10~~ wherein the substance interacts directly or indirectly with one or more amino acids selected from the group consisting of:
Gln322, Tyr323, Arg400 and Arg403.

13. (currently amended) A method according to claim 9~~, 10, 11 or 12~~ using a homologue of said model, wherein said homologue has a root mean square derivation from the backbone atoms of said amino acids of not more than 1.5 Å.

14. (currently amended) The method of claim 9~~, 10, 11, 12 or 13~~ wherein the substance is a small molecule.

15. (original) The method of claim 14 wherein said substance is cholesterol or a cholesterol derivative.

16. (original) A method for identifying an agonist or antagonist that binds to the LBD of RORα comprising:
(a) selecting a potential compound by performing rational drug design with one or more sets of atomic coordinates set forth in Table 8 or 9, wherein said selecting is performed in conjunction with computer modeling;
(b) contacting the potential compound with a LBD of RORα and
(c) measuring the biological activity of RORα.

17. (original) The method of claim 16 wherein said compound is designed to interact directly or indirectly with one or more amino acids selected from the group consisting of:
Cys321, Gln322, Tyr323, Leu328,Trp353, Cys356, Ala357, Lys359, Ile360, Glu362, Ala363, Val397, Phe398, Arg400, Met401, Arg403, Ala404, Val412, Tyr413, Phe414, Phe424, Leu427, Cys429, Phe432, Ile433, Val436, His517, Lys520 and Tyr540.

18. (original) A method according to claim 17 wherein the substance interacts directly or indirectly with one or more amino acids selected from the group consisting of:
Gln322, Tyr323, Arg400 and Arg403.

19. (original) The method of claim 18 wherein said compound is selected as RORα agonist if it stabilizes helix 12 of the LBD of RORα in the agonist position.

20. (original) The method of claim 19 wherein said compound is selected as RORα antagonist if it destabilizes helix 12 of the LBD of RORα from the agonist position.

21. (original) A pharmaceutical composition comprising a therapeutically effective amount of a compound stabilizing helix 12 of RORα in the agonist position and a pharmaceutically acceptable carrier.

22. (original) A pharmaceutical composition comprising a therapeutically effective amount of a compound destabilizing helix 12 of RORα from the agonist position and a pharmaceutically acceptable carrier.

23. (original) A method of screening for compounds interacting with RORα comprising:

(a) contacting RORα with a candidate compound,

(b) measuring interactions between the candidate compound and RORα in the absence of sterols, and

(c) selecting said compound if it interacts with RORα.

24. (original) The method of claim 23 for the screening for compounds useful for the treatment of cholesterol related diseases.

25. (original) The method of claim 23 for the screening for compounds useful for the treatment of endocrine disorders, atherosclerosis and cardiovascular diseases, metabolic diseases such as for instance obesity, inflammatory diseases, skin diseases, diseases related to the CNS, such as for instance Alzheimer disease and tumor related diseases.

26. (original) Use of RORα in cellular screening assays for the identification of compounds useful for the treatment of cholesterol related diseases.

27. (original) Use of RORα in cellular screening assays for the identification of compounds with endocrine disorders, atherosclerosis and cardiovascular diseases, metabolic diseases such as for instance obesity, inflammatory diseases, skin diseases, diseases related to the CNS, such as for instance Alzheimer disease and tumor related diseases.

28. (original) A composition comprising LBD of RORα and cholesterol or a cholesterol derivative.

29. (original) A composition according to claim 28 wherein said composition is crystallizable.

30. (new) The crystalline LBD of RORα of claim 2 wherein said LBD of RORα is associated with a lipophilic substance.

31. (new) The crystalline LBD of RORα of claim 2 wherein said crystal comprises a unit cell having the dimensions of a=55.9 Å ± 2 Å, b=49.9 Å ± 2 Å, c=60.7 Å ± 2 Å and β=98.7°±5° and space groupP2(1).

32. (new) The crystalline LBD of RORα of claim 3 wherein said crystal comprises a unit cell having the dimensions of a=55.9 Å ± 2 Å, b=49.9 Å ± 2 Å, c=60.7 Å ± 2 Å and β=98.7°±5° and space groupP2(1).

33. (new) The crystalline LBD of RORα of claim 2 wherein said crystalline LBD of RORα comprises the atomic structure coordinates of Table 8 or 9 or a part thereof.

34. (new) The crystalline LBD of RORα of claim 3 wherein said crystalline LBD of RORα comprises the atomic structure coordinates of Table 8 or 9 or a part thereof.

35. (new) A heavy atom derivative of a crystal according to claim 2.

36. (new) A heavy atom derivative of a crystal according to claim 3.

37. (new) A heavy atom derivative of a crystal according to claim 31.

38. (new) A heavy atom derivative of a crystal according to claim 32.

39. (new) A heavy atom derivative of a crystal according to claim 33.

40. (new) A heavy atom derivative of a crystal according to claim 34.